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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,903	06/21/2006	Alessandro Massimo Gianni	3765-0119US1	7353

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EXAMINER	
NIEBAUER, RONALD T	
ART UNIT	**PAPER NUMBER**
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	04/06/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/06/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/565,903	GIANNI ET AL.	
	Examiner	Art Unit	
	Ronald T. Niebauer	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 11-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/25/06 3/9/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 11-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11-14 refer to a state, condition or disease selected from a particular group. The members of the group do not fall within these categories. For example, tumor chemo-radiotherapy is not a state, condition, or disease. As claimed it is unclear for what/whom the method of treatment is designed.

Claims 15-16 refer to a combined preparation that is 'separately' administered. As claimed this is contradictory because if the preparation is 'combined' the components cannot be administered 'separately'.

Claim 2 refers to a combined preparation in which the components are administered 'simultaneously'. It is unclear how this claim further limits the first claim since there is no other way that a 'combined' preparation can be administered other than 'simultaneously'.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of using the composition as part of a treatment (for example, for mobilization of cells during the recovery phase of a disease or for mobilization of cells before/after organ or cell transplantation), does not reasonably provide enablement for the complete treatment of diseases such as forms of cancer for example non-Hodgkin lymphoma (NHL). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The scope of the claimed invention is open to patients in need that could be humans and animals (page 5 line 11). Since the preparation is open to include other components the preparation is broad in scope.

Working examples provide data on the mobilization of cells in patients including mice and monkeys. The working examples cover a very limited scope. The working examples do not involve any diseased patients, nor do the examples show any type of evidence that the composition itself is a method for treating a state, condition, or disease.

As claimed, the method is to treat states/conditions such as forms of cancer. It is well-known to one of skill in the art that cancer treatments are often unpredictable. In the cancer art it is difficult to translate in vitro data to living systems, but more importantly for this claimed invention it is difficult to translate data from non-diseased subjects to diseased subjects.

The state of the prior art shows that the treatment of specific forms of cancer, such as NHL, are unpredictable. Pettengell teaches that 'NHL is incurable with conventional chemotherapy' (page s1 column 2 first line). Pettengell teaches that autologous stem cell transplantation (ACST) has been used as part of a treatment regime in conjunction with chemotherapy. However, 'ACST in not curative' (page s2 column 1 line 10). The prior art also reveals that the use of GCSF and PlGF for the treatments of forms of cancer is underdeveloped. Although GCSF and PlGF have each been used for studies related to mobilization of stem cells, the combined use for the treatment of forms of cancer is not reported.

Experimentation is required in numerous areas particularly related to the treatment of a state, condition, or disease. There is no correlation provided as to how the mobilization of cells can translate to the treatment of specific diseases such as NHL. The claimed 'method' of treatment is simply the administration of the pharmaceutical composition. Typically, methods of treatment involve numerous steps. Since the pharmaceutical composition has not been tested on diseased patients or even tested in some type of model system, the effectiveness of the 'method' is unknown without experimentation. After this first line of testing, further experimentation includes tests in humans and determination of dosages to ensure that the effects are long lasting and not transient which can be a problem for the particular components of the composition.

In summary, a composition that can mobilize cells does not constitute in and of itself a method of treatment of a particular disease without supporting data. The claimed invention is broad, involves patient population in which results are often unpredictable, and the disclosure fails to provide a single working example in a diseased patient. For these reasons undue experimentation would be required to use the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Note that for purposes of this examination, claim 11 and dependent claims 12-14 although indefinite (see 112 2nd paragraph above) have been broadly interpreted as a method of treatment as well as a phase or step of a method of treatment. Claims 15-16 although indefinite (see 112 2nd paragraph above) have been interpreted as preparations such that GCSF and PlGF can be separately administered (and as though properly dependent from claim 1).

Claims 1-3, 11, 13, 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bahlmann et al. (US 2005/0272634) in view of Robinson et al.

Bahlmann et al. teach a pharmaceutical preparation containing GM-CSF and PlGF (for example, claim 41). In section 0058 the active ingredients are described as preferably being able to stimulate the mobilization of cells and include PlGF and/or GM-CSF. Bahlmann et al. teach the pharmaceutical composition to be used for parenteral administration (section 0054). Bahlmann et al. teach the use of the composition as part

of the therapy of diseases associated with a dysfunction of progenitor cells (section 0057) and for treatments of organ or tissue transplants before transplantation (section 0064).

Bahlmann et al. does not teach G-CSF, instead they teach GM-CSF. Further, Bahlmann et al. does not explicitly teach the use of recombinant forms or specific doses of GM-CSF or PlGF.

Robinson et al. teach that GM-CSF and G-CSF are functional equivalents and have been used for mobilization of stem cells (abstract). On page 535 (1st paragraph) it is stated that GM-CSF and G-CSF have been delivered to mobilize stem cells in the clinic. It is also pointed out (page 535 1st paragraph) that 'studies have compared the efficacy of similar daily doses of GM-CSF or G-CSF'. Robinson et al. teach that recombinant versions of G-CSF and GM-CSF are commonly used (abstract) and it would be obvious to one of skill in the art that these could be used interchangeably.

Starting with the work of Bahlmann et al. one would be motivated to substitute G-CSF for GM-CSF based on the teaching of Robinson et al. The composition described by Bahlmann can have other components so it meets the limitations of the current invention which includes G-CSF and PlGF but as claimed is open to containing other ingredients. Further Bahlmann et al. and Robinson et al. share the same goal – mobilization of progenitor cells. Taken together, it would have been obvious to one of skill in the art to make the compositions/use the methods of the current application and one would have an expectation for success.

Claims 1-4, 11, 13, 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bahlmann et al. and Robinson et al. as applied to claims 1-3, 11, 13, 17 above, and further in view of Carmeliet et al.(US 7105168) and Freireich et al.

Carmeliet et al. teach PlGF use as part of treatments such as transplantations (column 3 line 22) and specifically teach that recombinant PlGF is used (column 15 line 7) and PlGF dosages 'of 15ug/kg/day of active ingredient up to 100 ug/kg/day or higher' (column 15 line 12) are deemed to be a safe level.

Freireich et al. teach that doses of ingredients can be varied appropriately based on the patient and that quantitative calculations can be used as a starting point followed by routine optimization of dose amounts (page 220 2nd column 3rd paragraph).

The work of Carmeliet and Freireich provide details and specifics that would be obvious to one skilled in the art. In particular, recombinant proteins are often used in compositions and the doses that are used are based on what has been used previously at safe levels with further optimization. Since PlGF (Carmeliet et al.) and GCSF (Robinson et al.) have been described as being administered separately and motivation has been provided to combine them (see above, Bahlmann et al.) it would be obvious to one of skill in the art that the each component can be administered either 'separately' or simultaneously. Taken together, it would have been obvious to one of skill in the art to make the compositions/use the methods of the current application and one would have an expectation for success.

Claims 1-5, 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bahlmann et al., Robinson et al., Carmeliet et al., Freireich et al., as applied to claims 1-4, 11, 13, 15-17 above, and further in view of Kadar et al. (as cited in IDS).

Kadar et al. teach G-CSF use for cell mobilization and teach a specific dosage of 5ug/kg/day (page 611 abstract) twice a day for a total of 10ug/kg/day.

The work of Kadar, Carmeliet and Freireich provide details and specifics that would be obvious to one skilled in the art. In particular, recombinant proteins are often used in compositions and the doses that are used are based on what has been used previously at safe levels with further optimization. Taken together, it would have been obvious to one of skill in the art to make the compositions/use the methods of the current application and one would have an expectation for success.

Taken together, these references cover all elements of claims 1-5, 11-17. Taken together one would have an expectation for success since the modifications from Bahlmann et al. are minor and the references teach a common goal and safe dosages that have been used previously.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

Applicant is advised that should claim 3 be found allowable, claim 17 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). As noted above (112 1st paragraph) the term 'simultaneously' does not further limit a 'combined' preparation.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ronald T. Niebauer whose telephone number is 571-270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ZACHARIAH LUCAS
PATENT EXAMINER